

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problems Mailbox.**

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

| | |
|---|--|
| Date of mailing: 10 January 2002 (10.01.02) | |
| International application No.: PCT/GB00/03280 | Applicant's or agent's file reference: P24404/PPP |
| International filing date: 29 August 2000 (29.08.00) | Priority date: 28 August 1999 (28.08.99) |
| Applicant: STRACHAN, John, Scott | |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International preliminary Examining Authority on:
27 February 2001 (27.02.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

| | |
|--|--|
| <p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p> | <p>Authorized officer:</p> <p>J. Zahra</p> <p>Telephone No.: (41-22) 338.83.38</p> |
|--|--|

PATENT COOPERATION TREATY

PCT

COMMUNICATION OF
INTERNATIONAL APPLICATIONS

(PCT Article 20)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as designated Office

Date of mailing:

04 December 2001 (04.12.01)

The International Bureau transmits herewith copies of the international applications having the following international application numbers and international publication numbers:

International application no.:

PCT/GB00/03280

International publication no.:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer:

J. Zahra

Telephone No.: (41-22) 338.83.38

TENT COOPERATION TREAT)

PCTCOMMUNICATION IN CASES FOR WHICH
NO OTHER FORM IS APPLICABLE

From the INTERNATIONAL BUREAU

To:

PACITTI, Paolo
Murgitroyd & Company
373 Scotland Street
Glasgow G5 8QA
ROYAUME-UNI

| | |
|--|--|
| Date of mailing (<i>day/month/year</i>) 03 December 2001 (03.12.01) | |
| Applicant's or agent's file reference P24404/PPP | REPLY DUE see paragraph 1 below |
| International application No. PCT/GB00/03280 | International filing date (<i>day/month/year</i>) 29 August 2000 (29.08.00) |
| Applicant STRACHAN, John, Scott | |

1. ☐ REPLY DUE within _____ months/days from the above date of mailing
- ☐ NO REPLY DUE, however, see below
- ☒ IMPORTANT COMMUNICATION
- ☐ INFORMATION ONLY

2. COMMUNICATION:

The International Bureau regrets to inform the applicant that, due to a clerical error, the above identified international application has not been published promptly after the expiration of 18 months from the priority date, as provided in PCT Article 21(2)(a).

International publication will now take place on 10 January 2002 (10.01.02).

Meanwhile, the International Bureau will communicate a copy of the international application to each designated Office, in accordance with PCT Article 20.

A copy of this notification has been sent to the receiving Office RO/US and all designated Offices.

| | |
|---|---------------------------------|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland | Authorized officer R. Chrem |
| Facsimile No. (41-22) 740.14.35 | Telephone No. (41-22) 338.83.38 |

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

| | |
|--|------------|
| For receiving Office use only | |
| PCT/GB 00 / 03280 | |
| International Application No. | |
| 29 AUG 2000 | 29.08.2000 |
| International Filing Date | |
| United Kingdom Patent Office PCT International Application | |
| Name of receiving Office and "PCT International Application" | |
| Applicant's or agent's file reference (if desired) (12 characters maximum) P24404/PPP | |

* Title was changed, please see file

| | |
|---|--|
| Box No. I TITLE OF INVENTION | |
| "Molecular Resonance" 3 | |
| Box No. II APPLICANT | |
| Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) STRACHAN John Scott 6 Marchhall Crescent EDINBURGH EH16 5HN GB | |
| <input checked="" type="checkbox"/> This person is also inventor. Telephone No. --- Facsimile No. --- Teleprinter No. --- | |
| State (that is, country) of nationality: GB | State (that is, country) of residence: GB |
| This person is applicant for the purposes of: <input checked="" type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box | |
| Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S) | |
| Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) ADDED RO/GB | |
| This person is: <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.) | |
| State (that is, country) of nationality: | State (that is, country) of residence: |
| This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box | |
| <input type="checkbox"/> Further applicants and/or (further) inventors are indicated on a continuation sheet. | |
| Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE | |
| The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: <input checked="" type="checkbox"/> agent <input type="checkbox"/> common representative | |
| Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) PACITTI Paolo Murgitroyd & Company 373 Scotland Street GLASGOW G5 8QA GB | |
| Telephone No. 0141 307 8400 Facsimile No. 0141 307 8401 Teleprinter No. --- | |
| <input type="checkbox"/> Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent. | |

B x No V DESIGNATION OF STATES

The following designations are hereby ☒ under Rule 4.9(a) (mark the applicable check-box at least one must be marked):

☒ **Regional Patent**

- ☒ **AP** **ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, MZ Mozambique, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA** **Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP** **Eur pean Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA** **OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line).....

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- | | | | |
|--|---------------------------------------|---|--|
| <input checked="" type="checkbox"/> AE | United Arab Emirates | <input checked="" type="checkbox"/> KZ | Kazakhstan |
| <input checked="" type="checkbox"/> AG | Antigua and Barbuda | <input checked="" type="checkbox"/> LC | Saint Lucia |
| <input checked="" type="checkbox"/> AL | Albania | <input checked="" type="checkbox"/> LK | Sri Lanka |
| <input checked="" type="checkbox"/> AM | Armenia | <input checked="" type="checkbox"/> LR | Liberia |
| <input checked="" type="checkbox"/> AT | Austria | <input checked="" type="checkbox"/> LS | Lesotho |
| <input checked="" type="checkbox"/> AU | Australia | <input checked="" type="checkbox"/> LT | Lithuania |
| <input checked="" type="checkbox"/> AZ | Azerbaijan | <input checked="" type="checkbox"/> LU | Luxembourg |
| <input checked="" type="checkbox"/> BA | Bosnia and Herzegovina | <input checked="" type="checkbox"/> LV | Latvia |
| <input checked="" type="checkbox"/> BB | Barbados | <input checked="" type="checkbox"/> MA | Morocco |
| <input checked="" type="checkbox"/> BG | Bulgaria | <input checked="" type="checkbox"/> MD | Republic of Moldova |
| <input checked="" type="checkbox"/> BR | Brazil | <input checked="" type="checkbox"/> MG | Madagascar |
| <input checked="" type="checkbox"/> BY | Belarus | <input checked="" type="checkbox"/> MK | The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> BZ | Belize | <input checked="" type="checkbox"/> MN | Mongolia |
| <input checked="" type="checkbox"/> CA | Canada | <input checked="" type="checkbox"/> MW | Malawi |
| <input checked="" type="checkbox"/> CH and LI | Switzerland and Liechtenstein | <input checked="" type="checkbox"/> MX | Mexico |
| <input checked="" type="checkbox"/> CN | China | <input checked="" type="checkbox"/> MZ | Mozambique |
| <input checked="" type="checkbox"/> CR | Costa Rica | <input checked="" type="checkbox"/> NO | Norway |
| <input checked="" type="checkbox"/> CU | Cuba | <input checked="" type="checkbox"/> NZ | New Zealand |
| <input checked="" type="checkbox"/> CZ | Czech Republic | <input checked="" type="checkbox"/> PL | Poland |
| <input checked="" type="checkbox"/> DE | Germany | <input checked="" type="checkbox"/> PT | Portugal |
| <input checked="" type="checkbox"/> DK | Denmark | <input checked="" type="checkbox"/> RO | Romania |
| <input checked="" type="checkbox"/> DM | Dominica | <input checked="" type="checkbox"/> RU | Russian Federation |
| <input checked="" type="checkbox"/> DZ | Algeria | <input checked="" type="checkbox"/> SD | Sudan |
| <input checked="" type="checkbox"/> EE | Estonia | <input checked="" type="checkbox"/> SE | Sweden |
| <input checked="" type="checkbox"/> ES | Spain | <input checked="" type="checkbox"/> SG | Singapore |
| <input checked="" type="checkbox"/> FI | Finland | <input checked="" type="checkbox"/> SI | Slovenia |
| <input checked="" type="checkbox"/> GB | United Kingdom | <input checked="" type="checkbox"/> SK | Slovakia |
| <input checked="" type="checkbox"/> GD | Grenada | <input checked="" type="checkbox"/> SL | Sierra Leone |
| <input checked="" type="checkbox"/> GE | Georgia | <input checked="" type="checkbox"/> TJ | Tajikistan |
| <input checked="" type="checkbox"/> GH | Ghana | <input checked="" type="checkbox"/> TM | Turkmenistan |
| <input checked="" type="checkbox"/> GM | Gambia | <input checked="" type="checkbox"/> TR | Turkey |
| <input checked="" type="checkbox"/> HR | Croatia | <input checked="" type="checkbox"/> TT | Trinidad and Tobago |
| <input checked="" type="checkbox"/> HU | Hungary | <input checked="" type="checkbox"/> TZ | United Republic of Tanzania |
| <input checked="" type="checkbox"/> ID | Indonesia | <input checked="" type="checkbox"/> UA | Ukraine |
| <input checked="" type="checkbox"/> IL | Israel | <input checked="" type="checkbox"/> UG | Uganda |
| <input checked="" type="checkbox"/> IN | India | <input checked="" type="checkbox"/> US | United States of America |
| <input checked="" type="checkbox"/> IS | Iceland | <input checked="" type="checkbox"/> UZ | Uzbekistan |
| <input checked="" type="checkbox"/> JP | Japan | <input checked="" type="checkbox"/> VN | Viet Nam |
| <input checked="" type="checkbox"/> KE | Kenya | <input checked="" type="checkbox"/> YU | Yugoslavia |
| <input checked="" type="checkbox"/> KG | Kyrgyzstan | <input checked="" type="checkbox"/> ZA | South Africa |
| <input checked="" type="checkbox"/> KP | Democratic People's Republic of Korea | <input checked="" type="checkbox"/> ZW | Zimbabwe |
| <input checked="" type="checkbox"/> KR | Republic of Korea | <input type="checkbox"/> | Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet: |
| <input checked="" type="checkbox"/> KZ | Kazakhstan | <input type="checkbox"/> | |

In addition to the designations made above, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT, except the designation(s) of ~~the applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit).~~

Box No. VI PRIORITY CLAIMS ☐ Further priority claims are indicated in the Supplemental Box.

| Filing date of earlier application (day/month/year) | Number of earlier application | Where earlier application is: | | |
|---|-------------------------------|-------------------------------|---|---|
| | | national application: country | regional application: * regional Office | international application: receiving Office |
| item (1) 28 AUGUST 1999 28.08.99 | 9920351.5 | GB | | |
| item (2) | | | | |
| item (3) | | | | |

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): (1)

* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA)
(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA /

Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):

Date (day/month/year)

Number

Country (or regional Office)

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following number of sheets:

request : 3
description (excluding sequence listing part) : 22
claims : 4
abstract : 1
drawings : 7
sequence listing part of description : _____

Total number of sheets : 37

This international application is accompanied by the item(s) marked below:

1. ☐ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☒ other (specify): **Paents Form 23/77**

Figure of the drawings which should accompany the abstract: 1

Language of filing of the international application: **English**

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).


(Murgitroyd & Company)

For receiving Office use only

1. Date of actual receipt of the purported international application:

29 AUG 2000 29.08.2000

3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:

4. Date of timely receipt of the required corrections under PCT Article 11(2):

5. International Searching Authority (if two or more are competent): **ISA /**

6. ☒ Transmittal of search copy delayed until search fee is paid.

2. Drawings:

☒ received:

☐ not received:

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

13 SEPTEMBER 2000

(13.09.00)

127 OCT 2000

1

1 **Molecular Resonance**

2

3 The present invention relates to molecular resonance
4 of molecules, in particular molecular resonance
5 generated by laser radiation.

6

7 The concept of introducing high Q molecules that may
8 be stimulated by laser light to deliver toxic or
9 therapeutic effects is known from Dunlavy US5313315.
10 However, the direct stimulation of natural biological
11 processes by means of molecular resonance using
12 modulated or selective wavelength lasers has hitherto
13 proved to be impossible. This is because of the
14 scattering nature of the medium, the close proximity
15 of many resonances in natural molecules and the
16 difficulty of differentially raising the temperature
17 and thereby the reactivity of individual desired
18 molecules.

19

1 The present invention defines an apparatus and method
2 which overcomes some of these problems and covers the
3 nature and type of molecule susceptible to
4 differential stimulation.

5

6 Many critical chemical reactions in the body are
7 functions of the Cell Surface Cell Adhesion Molecules
8 that are in turn moderated by various integrins. The
9 geometric structure of many Cell Adhesion Molecules
10 and particular integrins is such that they are
11 capable of supporting a resonance at relatively low
12 frequency and surprisingly high Q. Unlike most
13 protein structures which are heavily damped or
14 inherently rigid in structure these molecules
15 generally take the form of a pair of relatively rigid
16 structures separated by space often bridged by a
17 single strand. This structure is especially sensitive
18 to periodic stimulation by a laser source especially
19 when the molecule surface is neutral or slightly
20 negatively charged. The polar and hydrophobic regions
21 of the molecule also differentially absorb energy
22 from laser light. This causes brief alterations in
23 both the structural bond energy and consequently
24 tends to amplify the vibration of the molecule. The
25 effect of this is to slightly increase the chemical
26 reactivity of particular molecules on a cell surface
27 relative to the surrounding molecules of a more
28 generally damped structure or other high Q molecules
29 of a different resonant frequency.

30

27 OCT 2000

1 In vivo the scattering of light at suitable
2 excitation wavelengths is extreme and as a result
3 even quite low frequency modulation signals tend to
4 be corrupted by the multiple scatter path lengths and
5 by the delay in absorption and release of photons in
6 those atoms at low energy states.

7

8 Also if continuous laser radiation is delivered to a
9 mass of cells the high damping factor of the
10 structure means that in general the overall
11 temperature of the cell mass rises. This occurs even
12 if modulated at the resonant frequency of a
13 particular molecule. The use of laser radiation in
14 this way produces an increase in the reactivity of
15 the entire cell surface which means that no actual
16 change in the reaction products occur because the
17 cells are in general, at equilibrium.

18

19 Conversely if very low energy is delivered at the
20 resonance frequency of the cell adhesion molecules or
21 if energy can be delivered as an intermittent pulse
22 of extremely short duration, the cell adhesion
23 molecules and the integrins with their inherently
24 high Q structure tend to maintain a slightly higher
25 temperature than the surrounding molecules. Thus the
26 cell adhesion molecules can be stimulated to a
27 greater reactivity than the surrounding surface
28 molecules.

29

1 Many biological processes can be disturbed into a
2 cascade of increasing reactivity if an initial
3 response is initiated. The immune response is a
4 powerful example of this but the nature of biological
5 reactions on the cell surface means that similar
6 cascade reactions occur for a wide variety of initial
7 conditions disturbed from equilibrium. Thus a very
8 small change in the reactivity of a surface molecule
9 for a short time can result in a dramatic change in
10 the chemistry of the cell surface for a considerable
11 period after the stimulation.

12

13 This effect depends on the cell chemistry being
14 substantially in equilibrium at the commencement of
15 the delivery of the radiation, otherwise the
16 resonance effect will tend to be swamped by the
17 current dominant reaction. Thus the target cells must
18 be in a relatively neutral pH environment and
19 obviously not engaged in a vigorous metabolic
20 process. Ideally also the cell surface molecule would
21 be neutral or slightly negative as this increases the
22 absorption of photons and so increases the transfer
23 of energy from the laser to the molecule.

24

25 Although this limits the use of this method, it has
26 one beneficial effect with respect to therapeutic use
27 in carcinomas. The undifferentiated cells of a
28 carcinoma are generally at equilibrium on the surface
29 as most of the chemical energy of the cell is

1 expended internally in the cell duplication process.
 2 This means that the undifferentiated cells of a
 3 carcinoma are particularly susceptible to the effect
 4 of the method on the surface chemistry since by their
 5 nature they conform to the ideal requirements for low
 6 energy disturbance of the equilibrium.

7

8 It is a critical requirement of this effect that the
 9 initial stimulation is periodic and of very low
 10 overall energy, as higher energy stimulation would
 11 merely raise the temperature of the entire cell by
 12 conduction and would not change the reaction
 13 equilibrium. To achieve such a change, individual
 14 molecules on the cell surface must be at different
 15 temperatures. Ideally it would consist of small,
 16 directed bursts of light modulated at the frequency
 17 of the desired molecule. Unfortunately it is clearly
 18 impossible to direct such a beam in the highly
 19 scattering medium of a living human body.

20

21 If a conventional laser or simple light beam is
 22 directed at a highly scattering medium, the
 23 modulation is eliminated at any substantial frequency
 24 because the light paths to any given point are so
 25 numerous and of such differing lengths that any
 26 modulation is reduced to noise after a few
 27 millimetres of the scattering medium. Even at lower
 28 frequencies the general level of overall energy
 29 delivered to the cells means that conduction and

1 convection tend to raise the overall temperature of
2 the cell surface rather than allow isolated
3 temperature differences to exist for any useful
4 length of time. Further it is impractical to generate
5 a light pulse which is of sufficiently short duration
6 and with a sufficiently high pulse repetition
7 frequency to be of practical use in the stimulation
8 of any resonance of a Q likely to occur in a living
9 cell surface molecule.

10

11 This invention provides a means of differentially
12 stimulating at least those molecules susceptible by
13 their structure to resonant stimulus.

14

15 The invention and preferred features thereof are
16 defined in the appended claims.

17

18 Embodiments of the invention will now be described,
19 by way of example only, with reference to the
20 drawings, in which:

21

22 Fig. 1 is a block diagram of an apparatus
23 embodying the invention;

24 Fig. 2 illustrates an interference pattern
25 produced by the apparatus of Fig. 1;

26 Fig. 3 shows the same interference in a scattering
27 medium;

1 Figs. 4 and 5 show typical cell adhesion
2 molecules;

3 Fig. 6 shows a human integrin molecule with a
4 single substantial high Q resonance;

5 Fig. 7 shows the zinc structure of the GAG protein
6 in the HIV virus; and

7 Fig. 8 shows a typical laser diode spectrum.

8

9 Referring to Fig. 1, the apparatus comprises a laser
10 diode 2 which is controlled by an amplitude modulator
11 1. The laser diode 2 is selected to have a
12 reasonably linear relationship between current and
13 wavelength with minimum mode hopping. The amplitude
14 modulator 1 modulates the current to the laser diode
15 2 which in turn results in a very small wavelength
16 modulation of the laser, for purposes discussed
17 below.

18 The output of the laser diode 2 is collimated by a
19 lens 3 and passed to an optical element 4. The
20 optical element 4 consists of a first diffraction
21 grating, a refractive element, and a second
22 diffraction grating such that the beam is
23 substantially cancelled. A preferred form of the
24 optical element 4 is as disclosed in WO97/22022 (now
25 EP-A1-0865618A and US-A-6064500). This allows the
26 cancellation to occur over a small percentage of the
27 wavelength variance of the laser source, rather than
28 at a single critical wavelength. Wavelengths beyond
29 the acceptance bandwidth of the cancelling optic 4

1 above and below the centre frequency pass without
2 being cancelled. This means that a complex Fresnel /
3 Fraunhofer zone will be generated, defined by the
4 beat frequency of the high and low frequencies as a
5 function of the aperture. This means that relatively
6 sparse zones of constructive interference will occur
7 between the high and low frequency passes of the
8 cancellation element in selected directions from the
9 aperture, as shown in Fig. 2.

10

11 As seen in Fig. 1, the optical element can be
12 adjusted angularly between positions 4A and 4B. This
13 varies the ratio of constructive to destructive
14 interference.

15

16 In effect the continuous beam is transformed into a
17 string of extremely short duration pulses typically
18 of sub femto second duration. The small wavelength
19 modulation of the laser diode 2 causes the
20 constructive and destructive nodes to move rapidly
21 through the volume of the Fresnel zone of the
22 collimator lens aperture. This has the effect of
23 simulating very short (sub picosecond) pulse
24 behaviour at any point in the Fresnel zone through
25 which the nodes pass at a pulse repetition frequency
26 defined by the amplitude modulator frequency.

27

28 The wavelength of the cancellation and constructive
29 interference zones for a theoretical single path

1 would be the difference between the two frequencies.
2 If the bandwidth of the cancelling element is narrow
3 this difference is very small and the effective
4 wavelength of the cancelled / non-cancelled cycle
5 would be very long, of the order of pico-seconds.
6 Therefore, the system would behave substantially
7 similarly to a system with no cancellation because it
8 requires an aperture much larger than the primary
9 light wavelength to generate a useful Fresnel /
10 Fraunhofer zone. Such an aperture would greatly
11 multiply the available Feynman diagram paths
12 eliminating any useful effect, even if it were
13 possible to generate a sufficiently coherent source
14 of such an aperture.

15

16 If the beat frequency can be made high enough the
17 wavelength of the cancelled to non-cancelled cycle
18 can be a fraction of a practical aperture. This will
19 make this wavelength sufficiently small to limit the
20 Feynman paths to within a cycle or two in free space
21 allowing the Fresnel / Fraunhofer effect to be
22 apparent. Since the centre frequency and spectrum
23 spread of a laser diode is easily modulated by
24 adjusting the current and or temperature of the
25 junction, the pattern of the Fresnel / Fraunhofer
26 zones can be varied dramatically by very small
27 variations in the wavelength of one or both pass
28 frequencies. Such modulation is produced in the
29 apparatus of Fig. 1 by the amplitude modulator 2.

30

1 Ideally the diode is modulated only slightly so that
2 the frequencies of the laser spectra move by an
3 amount smaller than that which would cause a second
4 lobe to spill outside the bandpass of the
5 cancellation element. As described above the aperture
6 of the apparatus has a dimension some substantial
7 multiple of the wavelength of the laser and some
8 significantly smaller multiple of the cancellation
9 cycle. Thus the number of different Feynman diagram
10 path lengths will be substantially less than infinite
11 for any given cycle length. Thus as different rays
12 from the laser take slightly different paths through
13 the optical element and thereafter cause the complex
14 Fraunhofer zone within the beam the pattern
15 generated is the inverse of a typical narrow spectrum
16 Fraunhofer zone.

17

18 Therefore, instead of the centre frequencies of the
19 beam being in general uncanceled, the centre
20 frequencies are totally cancelled. Thus instead of a
21 general constant level of light in the beam, the beat
22 frequency beam is characterised by isolated
23 relatively sparse "islands" of constructive
24 interference occurring in the generally cancelled
25 beam. Small variations in the centre frequency of the
26 laser as a result of modulation of the current or
27 temperature of the diode cause these islands of
28 constructive interference to move rapidly within the
29 beam.

30

1 Thus at any given point within the beam path, a
2 constructive interference node can be made to
3 modulate with respect to the modulation frequency of
4 the laser, irrespective of the scattering of the path
5 to that point. This is because few areas of
6 constructive interference exist in the initial beam
7 and while a constructive node can occur at any point
8 which happens to have suitable path lengths through
9 the scattering medium to the source, the initially
10 cancelled portion of the beam can not be
11 reconstructed to become a constructive node at any
12 point. Since the modulation of the laser changes the
13 locations of the constructive nodes at the modulation
14 frequency of the laser the result is that for any
15 point (or more accurately for the substantial
16 majority of points) within the beam a modulation
17 occurs irrespective of the scattering nature of the
18 medium. This is because the probability of a scatter
19 from one sparse node to a region where another sparse
20 node has existed within frequency of the modulation
21 is extremely low.

22

23 In a typical coherent beam, the presence of
24 constructive or destructive interference is of equal
25 likelihood and the modulation of the beam will
26 generally shift one constructive node only to be
27 replaced by another causing any initial modulation of
28 the beam to swamped by the noise of the multiple
29 paths. In contrast, the limiting factor for the
30 modulation frequency of a sparse constructive

1 interference beam is simply that the overall maximum
2 path length of any substantial probability in the
3 Feynman diagram. Path length is substantially shorter
4 than the wavelength of the modulation.

5

6 For a depth of five or six centimetres in human
7 tissue this allows frequencies in excess of 10 MHz to
8 be successfully modulated and in many human tissues
9 such as bone or neural tissue the depth would be
10 substantially greater or the limiting frequency
11 higher.

12

13 A conventional coherent or incoherent beam would have
14 high probability paths in the Feynman diagram. These
15 paths would overlap at very low frequencies (kHz) and
16 be of little practical use in the stimulation of
17 molecular resonance. It should be noted however that
18 the phenomena described above may be used as a means
19 to multiply the modulation frequency, up to the point
20 where the beam effectively becomes continuous. Thus
21 by careful selection of the aperture, the region of
22 the beam selected for transmission through the medium
23 and the modulation frequency it is possible to cause
24 the constructive nodes to pass across any given point
25 in the beam at frequencies many times higher than the
26 modulation frequency. In ideal conditions the
27 duration of exposure to a constructive node of any
28 point would be for a period equivalent to a quarter

27 OCT 2000

13

1 of the duration of a wavelength of the molecular
2 frequency repeated once per cycle.

3

4 If the wavelength of the laser is chosen to be one
5 easily absorbed by the atomic structures it is
6 desired to induce to resonance, then the beam will
7 efficiently deliver the desired modulation frequency
8 to the desired molecules. The energy of the beam is
9 extremely low but sufficiently high to differentially
10 raise the temperature of those molecules of
11 sufficient Q. Higher energy intensity would tend to
12 cause sufficient scatter even from the isolated
13 island nodes to swamp the modulation. Again the
14 result would be a general temperature increase rather
15 than the differential temperature increase of the
16 desired molecules.

17

18 Higher intensity can not significantly increase the
19 energy delivered to the desired molecules. Once the
20 probability of a single photon absorption at any
21 point on the molecule in a given and resonant
22 frequency cycle is exceeded, there is little
23 advantage in increasing the intensity since a second
24 photon will scatter without delivering more energy to
25 the given atom structure. The maximum temperature
26 difference that can be induced will be a function of
27 the damping factor and the Q of the resonant
28 component of the molecule. Therefore, increasing the
29 time of stimulation is pointless beyond some

1 reasonable multiple of the known time required to
2 initiate the reaction desired because the maximum
3 possible temperature variance will occur within a few
4 seconds.

5

6 The effect is therefore, only of merit in systems
7 where a small temperature variance can disturb the
8 equilibrium. Naturally this limits the range of
9 molecules that can be stimulated by this method. It
10 is fortunate however that many of the most usefully
11 stimulated molecules have exactly the characteristics
12 required. Most particularly the cell adhesion
13 molecules and integrins mentioned above. It should be
14 noted of course that all biological reactions occur
15 within a narrow temperature range and the progress of
16 most reactions can be varied quite significantly by
17 small temperature differences. It is of course a
18 natural consequence of light stimulation of a
19 molecular resonance that the molecular mode
20 temperature of the resonant structure will coincide
21 with the maximum valence state of the atoms since
22 they are in the process of absorbing and emitting
23 photons and so the electrons are in general at a
24 relatively high energy state. Naturally specific
25 photochemical reactions will be favoured and this may
26 either help or hinder the ability of the method to
27 stimulate a specific desired reaction depending on
28 the proximity of unwanted photochemical reaction
29 sites to the resonant stimulated sites. In designing
30 a specific stimulus these factors should be taken

27 OCT 2000

15

1 into account along with the equilibrium state and the
2 pH.

3

4 As stated above cell adhesion molecules and human
5 integrins such as Alpha 4 Beta 1 are ideally suited
6 for excitation to chemical activity by this method.

7

8 The stimulation of cell adhesion molecules and
9 integrins moderates a number of extremely useful
10 biological processes. Not least of these is cell
11 adhesion itself. It is obviously beneficial to
12 stimulate the adhesion molecules of a carcinoma as
13 the cell adhesion of carcinomas is relatively
14 depressed and enhancing the adhesion serves to reduce
15 the probability of metastasis. Such an effect would
16 be especially beneficial prior to the excision of a
17 tumour, reducing the likelihood of surgically
18 shedding carcinoma cells into the blood or lymph
19 system. The cell adhesion process and the integrins
20 especially Alpha 4 Beta 1 and Alpha 4 Beta 2 are
21 responsible not only for adhesion but also cell
22 recognition.

23

24 Bissel and Weaver have shown that by chemical
25 inhibition of adhesion sites of Alpha 4 Beta1, the
26 cell recognition can be moderated. It is therefore
27 possible to reduce an undifferentiated carcinoma cell
28 to its phenotype by correctly moderating the adhesion
29 reaction. The method used by Bissel and Weaver is

1 practical for in vitro application and can be used as
2 described in their patent for the measurement of
3 response to chemotherapy but it can not practically
4 be used in vivo. Conversely the laser radiation
5 method can be used in vivo and because of the
6 extremely low energies it is inherently safe at least
7 in terms of the radiation used. Care must of course
8 be taken to ensure that the stimulation delivered
9 will have a desirable consequence and much work is
10 needed to determine both the chemical responses that
11 are most easily stimulated and which of those are
12 desirable in a given case.

13

14 Gradually a library of reaction responses susceptible
15 to the stimulation will be developed from theory and
16 experiment and this library will be used to define a
17 range of reactions that are both of clinical use and
18 practical to stimulate. To date we have demonstrated
19 the stimulation of adhesion in leukocytes and neural
20 carcinomas. We have demonstrated substantial
21 moderation of cell surface chemistry in the prostate
22 gland.

23

24 This shows promise in the treatment of various
25 carcinomas. Stimulation of cell adhesion and
26 recognition alters the metabolism of the carcinoma
27 and causes induced, spontaneous apoptosis as a result
28 of undifferentiated cells communicating sufficiently.
29 This in turn causes the natural apoptosis of

27 OCT 2000

17

1 undifferentiated cells in an undifferentiated
2 environment. We have substantial evidence that like
3 Bissel and Weaver we have observed the reduction to
4 phenotype of undifferentiated cells and leukocytes.

5

6 Wayner US5730978 has shown an integrin-moderated
7 process which suggests that the method may have
8 application in the treatment of auto-immune diseases
9 and in the manipulation of the immune response in
10 general.

11

12 In vitro, the method can be used to alter the
13 chemistry of a variety of proteins and simple amino
14 acid structures in a manner that may be useful in the
15 production of pharmaceutical compounds and nutrition
16 products. Since the polar and hydrophobic components
17 of molecules have substantially different electron
18 populations, Quantum Electrodynamics (QED) shows that
19 these components differentially absorb energy from
20 photons. Coupled with a modulation frequency close to
21 one of the major axes of a given molecule, modulated
22 laser stimulation can be used to increase the
23 homogeneity of a population of proteins or simple
24 amino acid structures. This can be highly
25 advantageous since the metabolic absorption of amino
26 acid structures is moderated in vivo by shape
27 specific enzymes.

28

1 If a simple amino acid nutrient is made homogeneous
2 the number of enzymes required to metabolise the
3 nutrient is reduced. Again the cascade effect of cell
4 chemistry means that such a reduction in the
5 complexity of a particular chemical process can
6 dramatically increase the speed of absorption
7 sometimes by several orders of magnitude since the
8 required enzyme population is far more rapidly
9 manufactured. This is of critical importance in many
10 simple amino acid nutrients since they have a limited
11 life before they are broken down by incidental
12 chemical effects before they can deliver the required
13 effect to the target cells.

14

15 Under ideal conditions it will be possible to order
16 the folding of a protein to the desired biological
17 form by successive stimulation of suitable resonant
18 frequencies and the differential polar and
19 hydrophobic absorption of photons. Again the
20 application of a suitable modulated beam to a
21 sufficient volume of protein by conventional means
22 would be impossible as result of the scattering of
23 the light. The sparse constructive node beam
24 disclosed in the present application makes the
25 delivery of the required modulation a practical
26 possibility. A suitable array of the disclosed sparse
27 constructive node beams could be arranged on a
28 conveyor passing the proteins or simple amino
29 structures sequentially under the various modulation

27 OCT 2000

19

1 frequencies designed to favour each of the desired
2 folding steps.

3

4 Clearly much research would be required to determine
5 what modulations would be required to produce a
6 desired protein shape and it may be that in practice
7 very few proteins can be usefully manipulated in this
8 way. Such research is not within the scope of this
9 application; rather this application discloses a
10 method and apparatus capable of moderating aspects of
11 the folding process of proteins in a manner that can
12 be applied to a bulk mass for the first time. It is
13 extremely likely that a range of practical protein
14 structures can be generated by this method and it has
15 been shown by experiment that a population of
16 proteins or simple amino structures can be at least
17 made homogeneous which as mentioned above is useful
18 in itself.

19

20 In this regard it should be noted that the rotational
21 polarisation of the light source would cause
22 differential absorption of energy depending on the
23 "handedness" of a given molecular structure. In
24 addition, if the beam is modulated at the resonance
25 of a given structure, it is possible to either
26 enhance the production of one rotation of a molecule
27 versus the other. At slightly higher energy it is
28 possible to cause the destruction by a separate
29 chemical process of one or other rotation by

1 differentiating the temperature and therefore the
2 reactivity of one rotation versus the other. This is
3 a particularly useful application of the method as
4 many drugs and nutrients depend on only one form of
5 the molecule being present.

6

7 In this case of course the maximum Feynman path must
8 be very much shorter and so the maximum depth that
9 rotational polarisation effects would occur would be
10 no greater than a few millimetres in a typically
11 scattering medium. Hitherto no simple practical
12 method has existed to purify a population of
13 molecules to one or other rotation. The method
14 disclosed here provides a means of operating on bulk
15 media to generate a homogeneous single rotation
16 population or to allow a chemical process to
17 preferentially destroy one rotation relative to the
18 other in a mixed population of molecules.

19

20 The chemical consequences discussed herein of
21 molecular stimulation by sparse constructive node
22 techniques result primarily from the repeated
23 acceptance and release of photons by atoms at the
24 resonant frequency of the local atomic bonds or local
25 structure. There is a secondary effect on certain
26 molecular forms such as tetrahedral which can be
27 induced to spin provided the effective pulse length
28 is sufficiently short.

29

1 While the sparse constructive interference beam is
2 the primary thrust of the present application, it is
3 worth noting that the Hamiltonian solution to
4 Maxwell's equations suggest that cancelled light,
5 although carrying no energy in the conventional sense
6 in that it can not interact by conventional Quantum
7 Electrodynamics (QED) processes may have an effect on
8 the permittivity of free space and some theorists
9 suggest an effect on the strong nuclear force.
10 However since it can not scatter by QED effects this
11 has no detrimental affect on the efficiency of the
12 sparse constructive interference modulation and it
13 could be argued that the permittivity and nuclear
14 absorption effect, should it exist, would tend to
15 enhance the efficiency of the modulated frequency
16 coupling to the molecule. It should be noted that the
17 presence of the Hamiltonian effect has never been
18 satisfactorily proven and many theorists discount its
19 existence as a mere mathematical oddity, however we
20 note it here simply to point out that the effect
21 would tend to enhance rather than degrade the benefit
22 of the sparse constructive in interference effect.
23 The apparatus by its nature can therefor be used as a
24 means of delivering such a theoretical modulated
25 Hamiltonian "scalar" wave.

26

27 Figs. 2 to 8 illustrate elements of the foregoing in
28 more detail.

29

1 Fig. 2 shows the sparse constructive interference
2 effect from a 1 percent bandwidth cancellation plate
3 of 5 mm aperture. Black represents constructive
4 nodes.

5 Fig. 3 shows the same sparse constructive
6 interference in a scattering medium showing minimal
7 degradation of the effect and an increased path width
8 of majority destructive interference.

9

10 Figs. 4 and 5 show typical Cell Adhesion Molecules.
11 Both would have two primary resonances a high Q
12 resonance between the main elements at a relatively
13 low frequency and a higher frequency lower Q
14 resonance between the lobes of each element. The
15 molecule in Fig. 4 has a higher frequency resonance
16 between the main elements as it has some backbone
17 structure between the main elements.

18

19 Fig. 6 shows a human integrin molecule which will
20 have a single substantial high Q resonance defined by
21 the mass of the two main elements and the compliance
22 of the single backbone structure between the
23 elements. This molecule is extremely easy to resonate
24 sufficiently to moderate reactions and was the first
25 molecule to be successfully manipulated by the method
26 disclosed. This allowed an in vitro demonstration of
27 cell adhesion stimulated by laser stimulation
28 through a sparse constructive node cancellation
29 optical device. "Tracks" of adhered cell chains could

1 be generated in the beam path of the device in a
2 population of cells with substantially reduced
3 expression of the integrin and generally little
4 adhesion in the absence of the beam.

5

6 Fig. 7 shows the zinc "fingerlike" structure of the
7 GAG protein in the HIV virus. Again the molecule
8 shows the easily resonated dual element with
9 compliant single backbone bridge. This molecule is
10 much smaller and requires a higher energy and
11 resonant frequency. It was successfully resonated
12 with 470nm light using the method disclosed. It
13 should be noted that the chemical conditions around a
14 small viral particle are far harder to control or
15 predict and variable results are to be expected. Even
16 so substantial alterations in the processes of the
17 viral coat were observed and the viral penetration of
18 a cell population could be substantially altered.

19

20 Fig. 8 shows a typical laser diode spectrum, with a
21 typical cancelled portion of the spectrum and the
22 depth of the modulation that can be induced without
23 causing the nodes to spill outside the cancellation
24 zone and complicate the beat frequency pattern.

25 Different laser designs have different resonant modes
26 and these can be selected to obtain the most useful
27 range for a given application. Bragg gratings can be
28 used to stabilise the laser emission line and expand
29 the modulation amplitude that can be used while

1 keeping the overall frequency shift within the
2 required boundary. Lasers can be pulsed with short
3 duration pulses, which will produce an isolated
4 traverse though the frequency mode of the laser and
5 this can be determined to a high degree of
6 repeatability. If a Bragg grating is used with a
7 pulse laser the resulting frequency modulated pulse
8 will have a very high degree of control. The
9 combination of the short laser pulse and the rapid
10 resulting traverse of the sparse constructive nodes
11 means that a given point in the volume in front of
12 the laser will be exposed to extremely short (sub
13 picosecond) duration pulses. There are several
14 applications for such short pulses and conventional
15 methods for short pulse generation are relatively
16 costly.

1 CLAIMS

2

3 1. Apparatus for the stimulation of molecular
4 resonance by the application of very low intensity
5 electromagnetic radiation, comprising a laser of
6 multiple line cavity resonance consisting of a laser
7 diode with a collimated or near collimated beam, said
8 beam being passed through a phase cancellation
9 optical element having the characteristic of
10 cancelling several of the central lines of the laser
11 frequency while leaving the higher and lower
12 frequencies generally uncanceled such that the beat
13 frequency of the passed frequencies forms a pattern
14 of interference of constructive and destructive nodes
15 in which the diameter of the beam is set to be a
16 sufficiently low multiple of the wavelength of the
17 beat frequency to allow a substantial Fresnel zone to
18 be apparent in the beam and in which an aperture is
19 provided to select a portion of the Fresnel zone
20 wherein a substantial majority of destructive nodes
21 are apparent relative to the constructive nodes and
22 in which means are provided to modulate the laser
23 frequency.

24

25 2. Apparatus as claimed in Claim 1, wherein the
26 laser frequency is varied by adjusting the current on
27 a laser diode.

28

1 3. Apparatus as claimed in Claim 1 or Claim 2
2 wherein the laser frequency is varied by physical
3 alteration of a secondary cavity such as a crystal
4 provided to double the primary frequency.

5

6 4. Apparatus as claimed in any of the preceding
7 Claims wherein the modulation frequency is a harmonic
8 of the beat frequency.

9

10 5. Apparatus as claimed in any of the preceding
11 Claims wherein the modulation frequency is a harmonic
12 of a specific molecular resonance.

13

14 6. Apparatus as claimed in any of the preceding
15 Claims wherein the aperture or angle of the beam
16 passage through the cancellation device may be varied
17 consequently varying the beat frequency.

18

19 7. Apparatus as claimed in any of the preceding
20 Claims wherein the selected portion of the beam may
21 be varied to alter the balance between constructive
22 and destructive nodes.

23

24 8. Apparatus as claimed in any of the preceding
25 Claims wherein the means for modulating the laser
26 frequency is the consequential mode transition of a
27 laser diode in pulse mode.

1

2 9. Apparatus as claimed in Claim 8 where the laser
3 diode mode is held within bounds by reflection from a
4 Bragg grating so that the modulation of the Fresnel
5 zone nodes is a consequence of the Fourier transform
6 of the pulse.

7

8 10. A method of stimulation of molecular resonance
9 by the application of very low intensity
10 electromagnetic radiation modulated at resonant
11 frequencies of molecules of high Q by use of a laser
12 of multiple line cavity resonance consisting of a
13 laser diode with a collimated or near collimated
14 beam, said beam being passed through a phase
15 cancellation optical element said cancellation device
16 having the characteristic of cancelling several of
17 the central lines of the laser frequency while
18 leaving the higher and lower frequencies generally
19 uncanceled such that the beat frequency of the
20 passed frequencies forms a pattern of interference of
21 constructive and destructive nodes, in which method
22 the diameter of the beam is set to be a sufficiently
23 low multiple of the wavelength of the beat frequency
24 to allow a substantial Fresnel zone to be apparent in
25 the beam and in which an aperture is provided to
26 select a portion of the Fresnel zone wherein a
27 substantial majority of destructive nodes are
28 apparent relative to the constructive nodes and in
29 which means are provided to modulate the laser
30 frequency.

27 OCT 2000

28

1
2 11. Apparatus for the production of sub picosecond
3 light pulses, the apparatus comprising a laser
4 producing a collimated or near collimated beam, a
5 phase cancellation optical element through which said
6 beam is passed, said phase cancellation optical
7 element being formed by the series combination of a
8 first diffraction grating, a refractive element and a
9 second diffraction grating, whereby a pattern of
10 interference of constructive and destructive nodes is
11 formed in which the diameter of the beam is set to be
12 a sufficiently low multiple of the wavelength of the
13 beat frequency to allow a substantial Fresnel zone to
14 be apparent in the beam, the apparatus further
15 including means for pulsing the laser with short
16 duration pulses to produce for each pulse an isolated
17 traverse through the frequency mode of the laser.
18

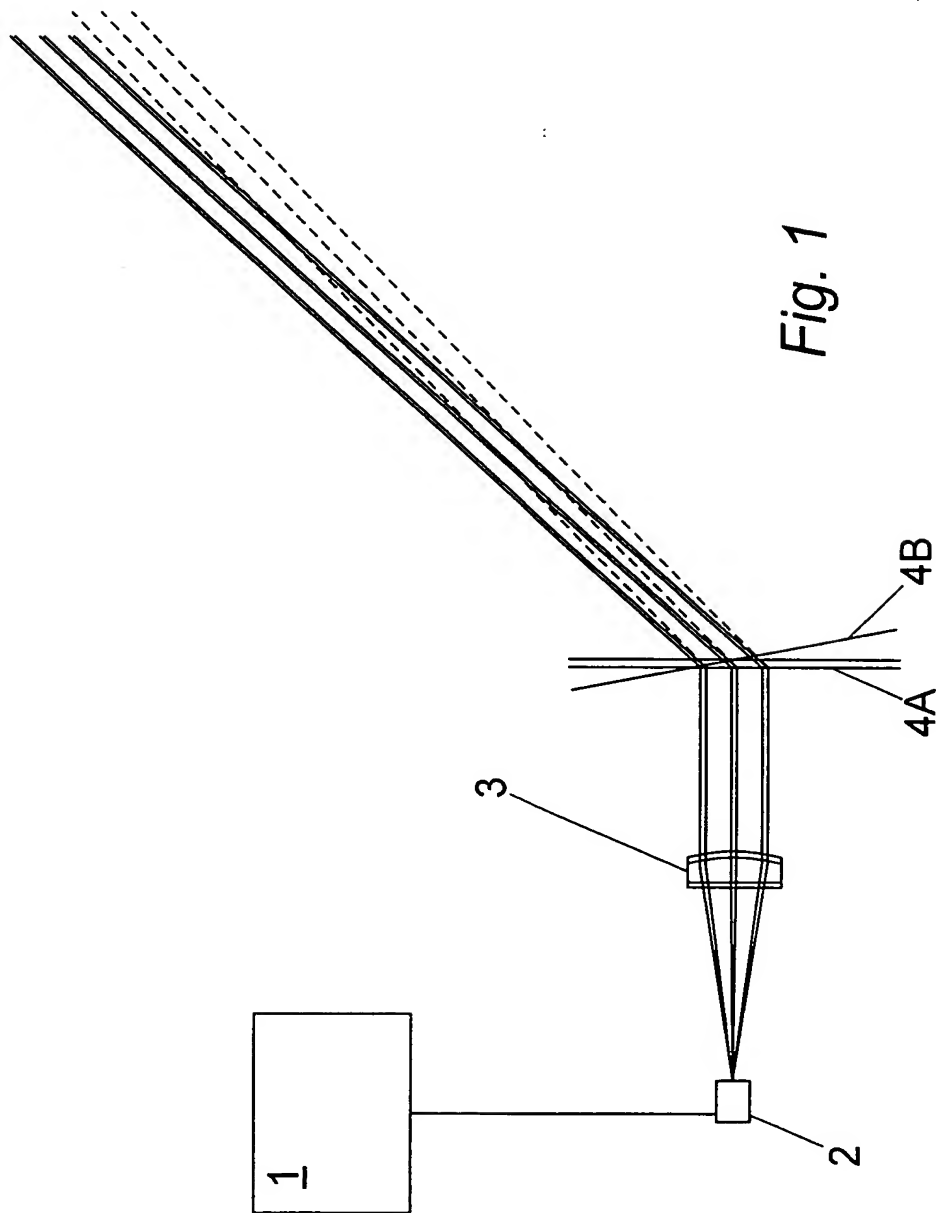
SUBSTITUTE SHEET (RULE 26)

1 ABSTRACT (Fig. 1)

2

3 This invention provides an apparatus comprising a
4 laser diode (2) whose wavelength is modulated by an
5 amplitude modulator (1). The laser output is
6 collimated by a lens (3) and passed through an
7 optical element (4) which contains two diffraction
8 gratings spaced by a refractive element. The
9 resulting output contains an interference pattern
10 which can be selected and controlled to interact with
11 chosen molecules so as to induce molecular resonance.

1 / 7



2/7

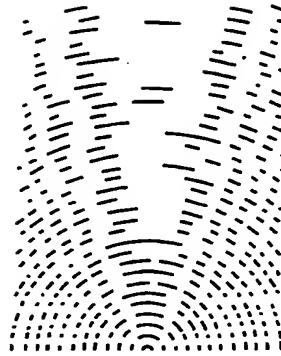


Fig. 2

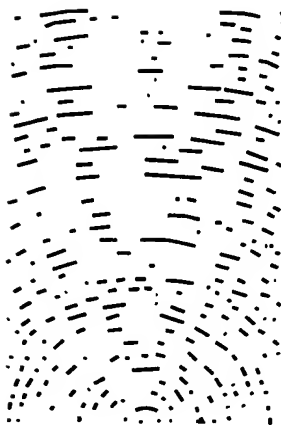


Fig. 3

3 / 7

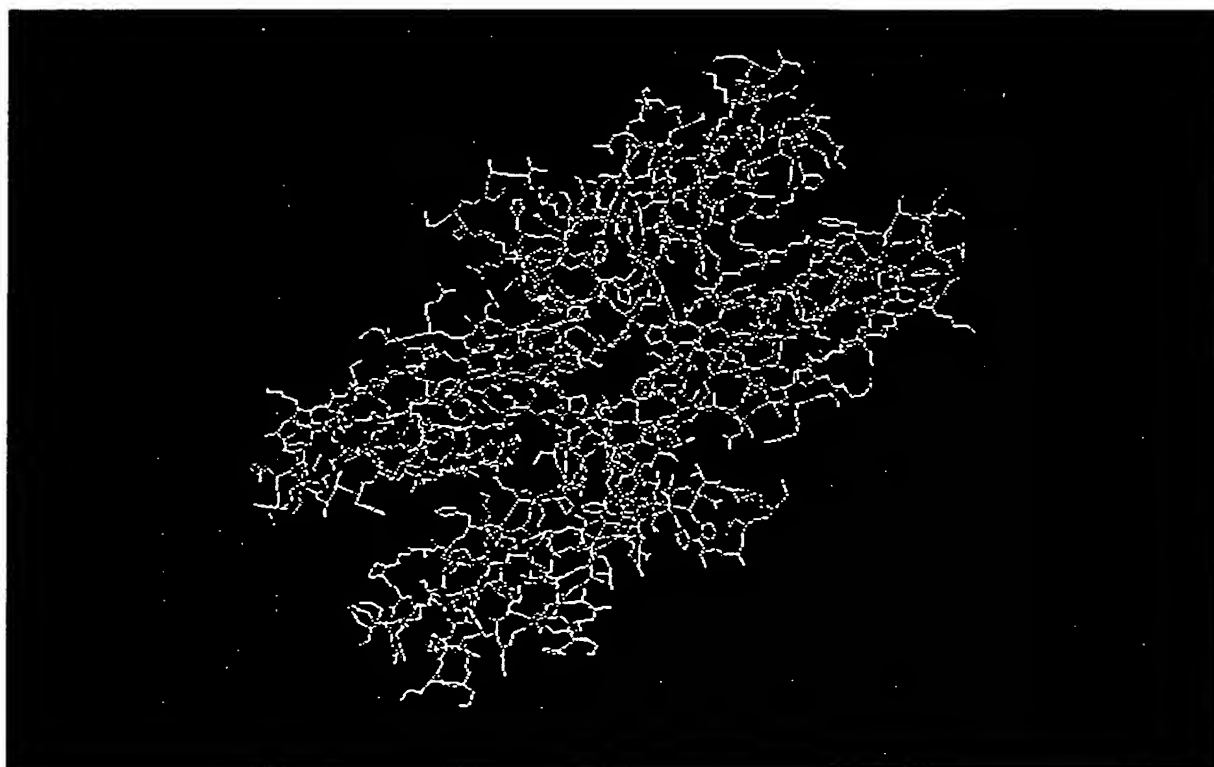


Fig. 4

4/7

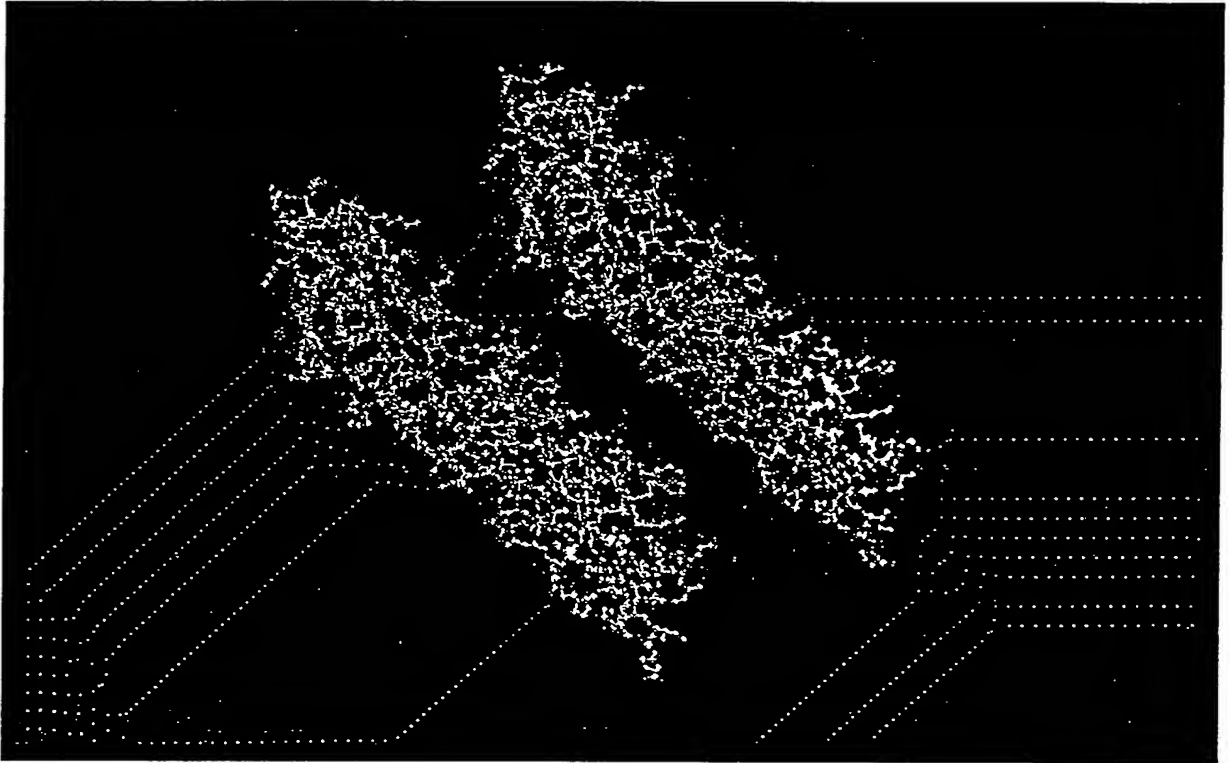


Fig. 5

5 / 7

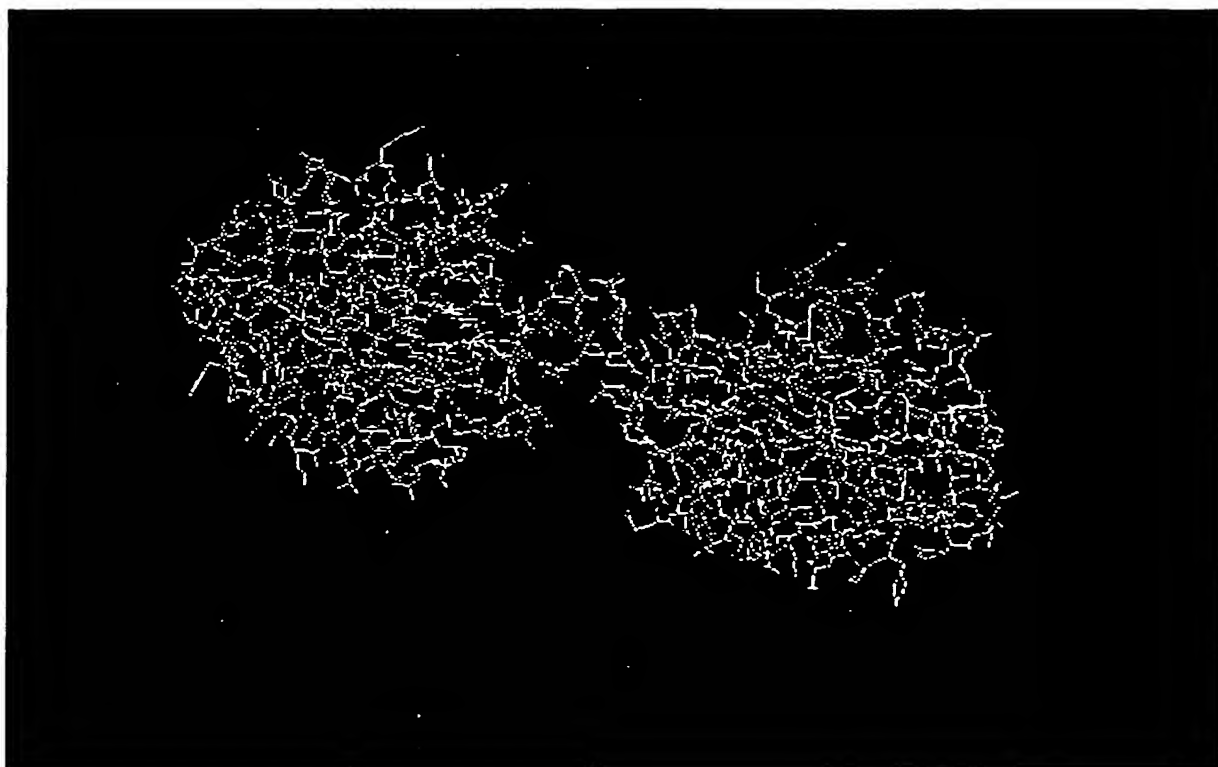


Fig. 6

6 / 7

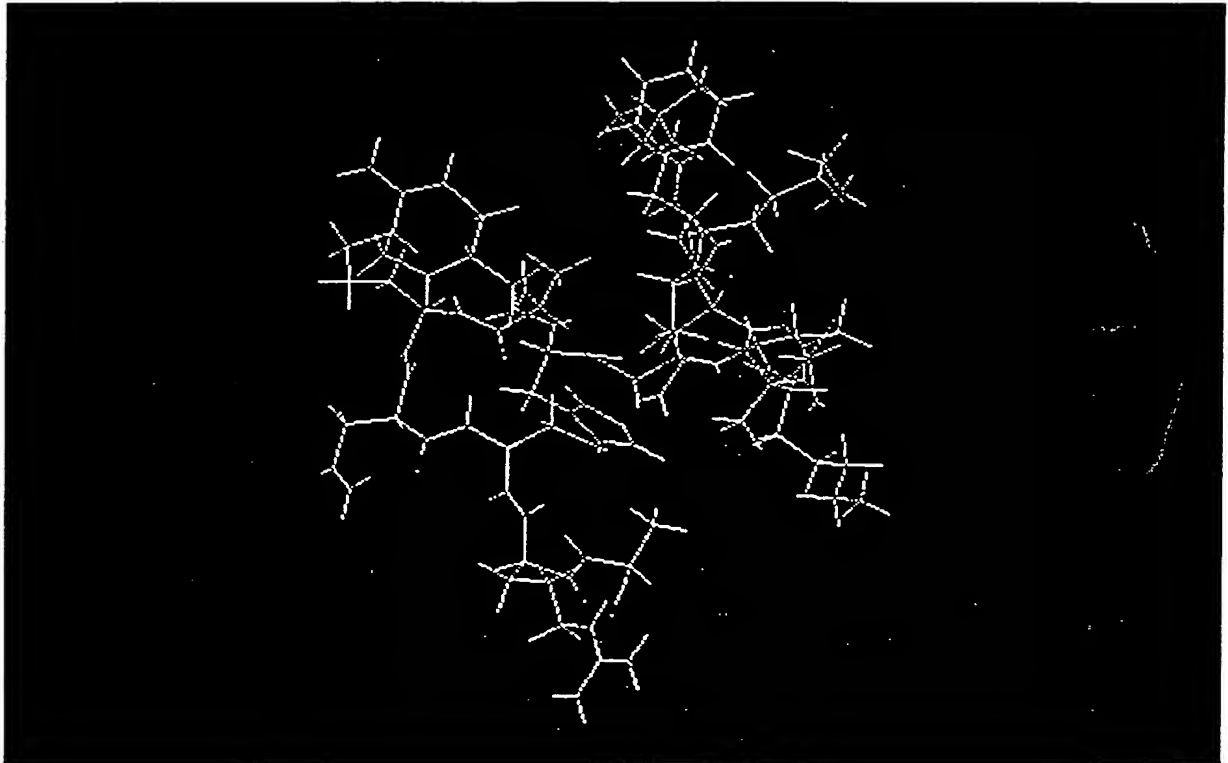


Fig. 7

7/7

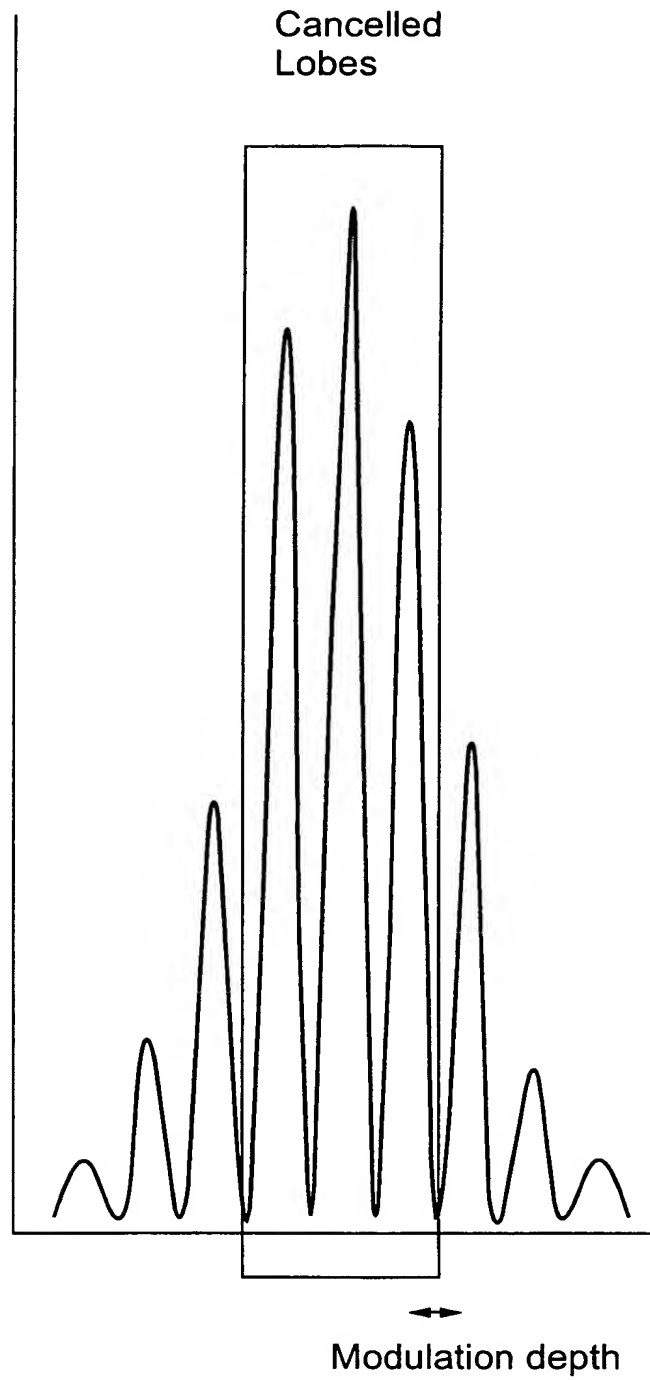


Fig. 8

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

REC'D 12 DEC 2000

WIPO

PCT

| | | |
|--|---|--|
| Applicant's or agent's file reference P24404/PPP | FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. | |
| International application No. PCT/GB 00/ 03280 | International filing date (day/month/year) 29/08/2000 | (Earliest) Priority Date (day/month/year) 28/08/1999 |
| Applicant STRACHAN, John, Scott | | |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

MOLECULAR RESONANCE STIMULATED BY LOW INTENSITY LASER LIGHT

5. With regard to the **abstract**,

the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.

1

None of the figures.

INTERNATIONAL SEARCH REPORT

Intern: val Application No

PCT/GB 00/03280

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61N5/067

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61N G02B H01S

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| A | WO 97 22022 A (STRACHAN JOHN SCOTT) 19 June 1997 (1997-06-19) cited in the application page 4, line 33 -page 9, line 10 ---- | 1, 10, 11 |
| A | US 5 658 234 A (DUNLAVY JOHN HAROLD) 19 August 1997 (1997-08-19) column 2, line 28 - line 67 ---- | 1 |
| A | US 4 834 474 A (GEORGE NICHOLAS ET AL) 30 May 1989 (1989-05-30) abstract ---- | 1, 10, 11 |
| A | US 4 536 883 A (CHAPLINE JR GEORGE F) 20 August 1985 (1985-08-20) column 1, line 32 - line 50 ----- | 1, 10, 11 |



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

5 December 2000

Date of mailing of the international search report

12/12/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Petter, E

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/03280


| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
|---|---|---------------------|--|--|
| WO 9722022 | A | 19-06-1997 | AU 7704296 A CA 2239833 A EP 0865618 A US 6064500 A | 03-07-1997 19-06-1997 23-09-1998 16-05-2000 |
| US 5658234 | A | 19-08-1997 | NONE | |
| US 4834474 | A | 30-05-1989 | NONE | |
| US 4536883 | A | 20-08-1985 | NONE | |

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| | | | |
|--|---|---|--|
| Applicant's or agent's file reference P24404A/AHO/PPP | | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) | |
| International application No. PCT/GB00/03280 | International filing date (day/month/year) 29/08/2000 | Priority date (day/month/year) 28/08/1999 | |
| International Patent Classification (IPC) or national classification and IPC A61N5/067 | | | |
| Applicant STRACHAN, John Scott | | | |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p> | | | |
| <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application | | | |
| Date of submission of the demand 27/02/2001 | | Date of completion of this report 09.11.2001 | |
| Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | | Authorized officer Abraham, V Telephone No. +49 89 2399 7463 | |



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/03280

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):
Description, pages:

1-22 as originally filed

Claims, No.:

1-11 as originally filed

Drawings, sheets:

1/7-7/7 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/03280

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-11.

because:

☒ the said international application, or the said claims Nos. 10 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-9,11 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

III

1. According to Article 34(4)(a)(i) PCT and Rule 67.1 PCT no international preliminary examination is required to be carried out on claim 10 of the present application, because the subject-matter of this claim relates to a method for treatment of the human or animal body by therapy (see page 4, lines 16-26).
2. The set of claims does not meet the requirements of Article 6 PCT. Although claims 1 and 11 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter. The set of claims as a whole therefore lacks conciseness. Moreover, lack of clarity arises, since the plurality of independent claims makes it difficult, if not impossible, to determine the matter for which protection is sought and, consequently, no further examination of claims 1-9,11 with regard to novelty and inventive step can be carried out. The claims should have been redrafted to contain a single independent claim.
3. An examination of claims 1-9,11 with regard to novelty and inventive step is furthermore not possible, because of the following severe clarity objections:
 - 3.1 According to the description (page 4, lines 28 -page 5, line 7) it is a critical and essential requirement of the present invention that the intensity of the electromagnetic radiation is "very low", in order to selectively stimulate desired molecules.
However, the term "very low intensity" used in claim 1 and implicitly also in claim 11 is vague and unclear, has no well-recognised meaning and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).

Since no definition of this unclear term is to be found in the specification of the present application, the invention does not appear to be disclosed in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art. Therefore, an objection according to Article 5 PCT may be raised unless the applicant proves, that the intensity necessary for achieving the desired effect is derivable from the disclosure of the present application without the exercise of inventive skill.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/03280

3.2 Claims 1 and 11 further do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved which merely amounts to a statement of the underlying problem ("the diameter of the beam is set to be **a sufficiently low multiple of the wavelength of the beat frequency to allow a substantial Fresnel zone to be apparent**"). The technical features necessary for achieving this result should be added. This does not appear to be possible, because the result itself, namely the term "substantial Fresnel zone", is vague and unclear.

Again, no clarification is to be found in the specification of the present application, and the invention does one more time not appear to be disclosed in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art. A second objection according to Article 5 PCT may be raised unless the applicant proves, that the beam diameter necessary for achieving the desired effect is derivable from the disclosure of the present application without the exercise of inventive skill.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| | | |
|--|---|--|
| Applicant's or agent's file reference P24404/PPP | FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. | |
| International application No. PCT/GB 00/ 03280 | International filing date (day/month/year) 29/08/2000 | (Earliest) Priority Date (day/month/year) 28/08/1999 |
| Applicant STRACHAN, John, Scott | | |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

MOLECULAR RESONANCE STIMULATED BY LOW INTENSITY LASER LIGHT

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☒ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

1
☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

GB 00/03280

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61N5/067

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61N G02B H01S

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| A | WO 97 22022 A (STRACHAN JOHN SCOTT) 19 June 1997 (1997-06-19) cited in the application page 4, line 33 - page 9, line 10 --- | 1, 10, 11 |
| A | US 5 658 234 A (DUNLAVY JOHN HAROLD) 19 August 1997 (1997-08-19) column 2, line 28 - line 67 --- | 1 |
| A | US 4 834 474 A (GEORGE NICHOLAS ET AL) 30 May 1989 (1989-05-30) abstract --- | 1, 10, 11 |
| A | US 4 536 883 A (CHAPLINE JR GEORGE F) 20 August 1985 (1985-08-20) column 1, line 32 - line 50 ----- | 1, 10, 11 |



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

* & * document member of the same patent family

Date of the actual completion of the international search

5 December 2000

Date of mailing of the international search report

12/12/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Petter, E

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

GB 00/03280

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|--|--|
| WO 9722022 A | 19-06-1997 | AU 7704296 A CA 2239833 A EP 0865618 A US 6064500 A | 03-07-1997 19-06-1997 23-09-1998 16-05-2000 |
| US 5658234 A | 19-08-1997 | NONE | |
| US 4834474 A | 30-05-1989 | NONE | |
| US 4536883 A | 20-08-1985 | NONE | |